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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,919	03/17/2000	Steven Neville Chatfield	KCO1002US	3175

7590 07/08/2002

Thomas e Popovich & Wiles PA
IDS Center
80 South 8th Street
Suite 1902
Minneapolis, MN 55402-2111

EXAMINER	
LI, BAO Q	
ART UNIT	**PAPER NUMBER**
1648	19

DATE MAILED: 07/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/527,919	CHATFIELD, STEVEN NEVILLE	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 35-46 are pending.

Declaration

The Declaration filed on 04/24/200 as part of paper No. 16 is acknowledged.

Response to the Amendment

This is a response to the amendment B, paper No. 18, filed 04/24/02. Claims 1-34 have been canceled. New claims 35-46 have bee added.

Please note any ground of rejection that has not been repeated is removed. The text of those sections of Title 35,US.Code not included in this section can be found in a prior office action.

Claim Rejections - 35 USC § 103

Claims 35-46 corresponding to the canceled claims 1-4, 10, and 18 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Mimms et al. (EP-A-0 389 983), Khan et al. (WO 94/03615) and Shi et al. (Vaccine 1995, Vol. 13, pp. 933-937).

In response to the office action, Applicants filed a Declaration signed by Dr. Page. However, it is not found persuasive to overcome the rejection.

Applicants argue through Dr. Page's Declaration that there are a vast number of combinations of carrier and antigenic sequence that could in theory have been dreamt up by a person skilled in the art. Out of all these possible combinations, there was no motivation in the art whatsoever to focus on both fragment C and pre-S1 and put them together. This specific selection was not an obvious selection when viewed in the "real life" context of all the other combinations that a person skilled in the art might in theory have put together.

Applicant's arguments have been fully considered but they are not persuasive because the tetC used as a carrier protein with different antigens has been known in the art as evidenced by Khan et al., they explicitly teach that Tetanus toxoid C (tetC) has been extensively used as an adjuvant and the result of recombinant antigen has been shown to have good and enhanced immunogenicity when a gene coding for a protein antigen is linked to the gene for tetanus toxin C fragment (line4 on page 3 through line 8 on page 4). Khan et al. also point out that several

viral antigens, such as HIV, hepatitis A or B et al. are suitable for making a fusion protein with tetC as a good vaccine candidate for inducing a protective immunity against HBV (page 5, line 10 through page 6, line 4).

In addition, the epitopes of HBV pre-S1 protein as a subunit vaccine antigen is also well documented by Mimms et al. For example, they teach several immunogenic epitopes of HCV pre-S1 or Pre-S2 for as antigens to produce the anti-pre-S1 and pre-S2 antibodies (see example 4). In order to get better immunity for the subunit HBV surface antigen, the art also teach to use a carrier protein as adjuvant to fused with the short peptide of HBV surface antigen to stimulates the immune response.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to come the teaching of Khan et al. Minmms etal. and Shi to make a HBV pre-S1 fusion protein with teteC to induce an immune response with highly expected result.

Since there is no unexpected results, it is still concluded that the claimed invention as a whole is prima facie obvious absence unexpected results.

New grounds of rejection

Claim Rejections - 35 USC § 112

Claims 35-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for constructing an immunogenic composition comprising the fusion peptide consisting of pre-S1 HBV peptide (pre S1 $_{ayw}$ 20-47 or pre S1 $_{ayw}$ 120-147) fused with the full length of the tetanus toxin fragment C to induce antibody response, does not reasonably provide enablement for having an immunogenic composition made by fusing HBV pre-S1 in any length of at least 6 amino acids with tetanus toxin fragment C in any length short than the full length or at least 6 contiguous amino acids of tetanus toxin fragment C . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed

Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988).

The recombinant HBV vaccines comprising either single HBV S antigen or a triple antigen (S, pre-S1 and pre-S2) have been used for as vaccines for almost 2 decades. However, a recent comparative study of a triple antigen and a single antigen recombinant vaccine for adult has demonstrated that the single antigen of HBV vaccine produce less protective immunity (83%) than the triple antigen vaccine of HBV (97%) as evidenced by Young et al (J. Med. Virol. 2001, Vol. 64, pp. 290-298, see abstract), indicating the unpredictability of using single HBV pre-S1 or its fragment along as an immunogene. Because of this, the art teach to use a carrier protein to fuse with HBV subunit antigen as an adjuvant in order to enhance the immunity of HBV subunit surface antigen as evidenced by Shi et al. (Vaccine 1995, Vol. 13, pp. 93-937). However, it is unpredictable whether each of designed fusion protein is able to produce an enhanced immunity. For example, the fusion protein of pTECH3/S1/S2(preS1$_{ayw}$21-47/preS2$_{ayw}$1-55$_{aa}$) as disclosed in the specification does not produce an antibody against S1(20-47, see Table 2 on page 18).

In the instate case, Applicants only teach that a full length toxin C fragment fused with pre-S1(pTECH3/S1: pre S1 $_{ayw}$ 20-47 and pTECH3/SB: pre S1 $_{ayw}$ 120-147and) is able to induce an anti-pre-S1 antibody in mice. However, there is no teaching whether the pre-S1 fused with other fragment of toxin C except its full length, such as only 6 amino acids, is able to produce an enhanced immunity. Because the specification lack the teaching about which contiguous amino acids of toxin C are necessarily required, it is, therefore, considered a undue experimentation would have been required to enable the intended claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
June 28, 2002

ALI R. SALIMI
PRIMARY EXAMINER